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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD,
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(54) Title: **NEW GDF-9 AND GDF-9B (BMP-15) SEQUENCES FOR ALTERING MAMMALIAN OVARIAN FUNCTION AND OVULATION RATE**

(57) Abstract: The present invention provides compositions and methods for modulating the ovulation rate and therefore fertility in female mammals including humans. The invention also relates to novel mutations in the GDF-9 and GDF-9B genes which are associated with changes in fertility.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/NZ03/00109

A. CLASSIFICATION OF SUBJECT MATTERInt. Cl. ⁷: C12N 015/12; A61K 038/16, 039/395; A61P 015/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

SEE ELECTRONIC DATABASE BOX BELOW

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SEE ELECTRONIC DATABASE BOX BELOW

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

AGRICOLA CA MEDLINE WPIDS: GDF-9? GDF9? BMP15 BMP-15 FERTIL? INFERTIL? OVULAT? BREED?
 IMMUNIS? VACC? OOCYTE? FOLLIC? FECUND? PROLIFICACY OVAR? CORPUS LUTEUM CONTRACEPTI?
 SEQ ID NOs 6, 12 AND 18

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/85926 A2 (AGRESEARCH LIMITED) 15 November 2001. See the entire document.	2, 7-11, 13, 14, 17, 19-37, 41-43
Y		1, 2, 11-22, 34-37, 41-43
X	WO 01/96393 A2 (AGRESEARCH LIMITED) 20 December 2001. See the entire document.	2, 7-11, 13, 14, 17, 19-38, 41-43
Y		1, 2, 11-22, 34-37, 41-43

☒ Further documents are listed in the continuation of Box C
 ☒ See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

 Date of the actual completion of the international search
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INTERNATIONAL SEARCH REPORT

International application No.

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	Juengel JL et al (2002). Growth differentiation factor 9 and bone morphogenetic protein 15 are essential for ovarian follicular development in sheep. <i>Biology of Reproduction</i> 67: 1777-1789. See the entire document.	23-33, 38 1, 12, 15, 16, 18-22, 34-37, 41-43
X	WO 99/17797 (THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE) 15 April 1999. See the entire document.	23, 24, 26-29, 31-33
X	Vitt UA et al (2000). <i>In vivo</i> treatment with GDF-9 stimulates primordial and primary follicle progression and theca cell marker CYP17 in ovaries of immature rats. <i>Endocrinology</i> 141: 3814-3820. See the entire document.	23, 24, 27
X Y	WO 00/66620 (CREATIVE BIOMOLECULES INC) 9 November 2000. See the entire document.	38 1, 12, 15, 16, 18-22, 34-37, 41-43
X Y	Yan C et al (2001). Synergistic roles of bone morphogenetic protein 15 and growth differentiation factor 9 in ovarian function. <i>Molecular Endocrinology</i> 15: 854-866. See the entire document.	39, 40 1, 12, 15, 16, 18-22, 34-37, 41-43
X Y	Montgomery GW et al (2001). Genes controlling ovulation rate in sheep. <i>Reproduction</i> 121: 843-852. See the entire document, and in particular the abstract and page 849-851.	1, 3-6, 12, 15, 16, 18-22, 34-37, 41, 43 2, 11, 13, 14, 17, 19-22, 34-37, 41-43
	Note: for the Y indications, either WO 01/85926 or WO 01/96393 may be combined with any one of Juengel et al (2002), WO 00/66620 or Yan et al (2001) (with relevance to claims 2, 11, 13, 14, 17, 19-22, 34-37 and 41-43) or with Montgomery et al (2001) (with relevance to claims 1, 12, 15, 16, 18-22, 34-37 and 41-43).	

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos :
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos : 38 (in part)
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
The claim does not comply with Rule 6.3 of the PCT, because this claim recites analogues or antagonists of GDF-9 or GDF-9B, which owe nothing to the applicant's invention and do not define the technical features of the invention. The search on this claim has been restricted to analogues and antagonists derived specifically using GDF-9 or GDF-9B. The full scope of these claims has not been searched.
3. ☐ Claims Nos :
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

International application No.

PCT/NZ03/00109

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
WO	01/85926	AU	608210	CA	2408051	EP	1292674
		NZ	500844				
WO	01/96393	AU	6795001	CA	2410532	EP	1294755
		NZ	502796				
WO	99/17797	AU	1071499	AU	757563	CA	2306452
		EP	1021201	JP	2001518516T		
WO	00/66620	AU	4676600	CA	2371695	EP	1181041